REMARKS

By the foregoing amendment, applicant has presented new independent claim 34, which is similar to previous claim 1, but recites that the therapeutic agents (i-xiii) are provided in particulate dosage form "selected from the group consisting of a propellant-containing dosage aerosol, an inhalation powder, or a propellant-free inhalation suspension".

Support for the foregoing amendment can be found in the original disclosure, for example at page 4, lines 26-31 of the Specification. Accordingly, the foregoing amendment does not raise the issue of new matter.

Reconsideration and withdrawal of all the previous rejections are respectfully requested in view of the following comments.

Initially, applicants appreciate the Examiner's withdrawal of the previous rejection of the claims under 35 U.S.C. 102(e) as allegedly anticipated by Meade et al (U.S. Patent Publication 2003/0018019 A1).

However, in view of the foregoing amendments and the following comments, applicants respectfully submit that the present claims 1-9, 15-26 and 34 are also patentable over Meade et al. in view of Foulds et al. (Pharmaceutisch Weekblad Scientific Edition, 1983 Vo. 5, pages 74-76) under 35 U.S.C 103 (a). In view of the Examiner's comments appearing on page 10 of the preceding Office Action that "a recitation of the intended use of claimed invention must result in a structural difference between the claimed invention and prior art in order to patentably distinguish the claimed invention from the prior art" applicants present new independent claim 34. Applicants respectfully submit that new independent claim 34 is a structural difference in reciting that the therapeutic agents (i)-(xiii) are provided in particular dosage form selected from the group consisting of a propellant-containing dosage aerosol, an inhalation powder and

a propellant-free inhalation suspension" having a particle size from nano-size up to about 12 μm for combinations (i-ix) and (xiii) individually and for the combinations (x)-(xii) approximately 95% of the active particles have a particle size of below 2.5μm, and the remaining particles have a particle size of between 2.5 and 5μm.

Thus, for elected species (xii) 100% of the particles are smaller than 5μm and of those 95% of all particles have particles size below 2.5μm in the specified dosage form. No such teaching can be gleaned from the proposed combination of Meade et al. in view of Foulds et al for the reasons as either set forth in the Office Action, or for any other reason.

Contrary to what the Examiner alleges, there is "no explicit disclosure in Meade et al. of a pharmaceutical product comprising any of the claimed combination of active ingredients where the active ingredients have a particles size range of from nano-size up to about 12μm as recited in the present claims".

The Examiner concedes as much in the first full paragraph on page 12 of the Office Action which states "Meade et al. do not explicitly teach that applicant's elected species (i.e. combination xii) is a composition where approximately 95% of the active particles have a particle size of below 2.5μm and the remaining particles have a particle size of between 2.5. and 5μm". The Examiner cites the Foulds et al publication in combination with Meade et al in order to correct this forgoing deficiency.

However, Foulds et al is directed to "nebulizers". As is well known to those having ordinary skill in the art nebulizer is a "atomizer; a device for throwing a spray" see the attached page 1020 from Dorland's Illustrated Medical Dictionary Twenty-fifth Edition W.B. Saunders Philadelphia (1974). A spray is of course "a liquid minutely divided or nebulized by a jet of air or steam"; See page 1461 from the same attached Dictionary.

New independent claim 34 clearly avoids even the existence of a spray or a

minutely divided liquid by its recitations of particulate dosage form. However, each of claims 1-9 and 15-26 are also distinguished by these same facts.

Foulds et al. is directed to a minutely divided liquid e.g. a solution which has been nebulized. The Examiner simply fails to comprehend what Foulds et al is teaching as compared to the difference in the claimed invention.

Foulds et al is addressing the particle size of a liquid i.e., the minutely divided liquid or the nebulized material shown in the lung scans of figure 1 as appears on page 75, which has nothing at all to do with the particle size of the particulates of elected species (xii) or any of the other species (i)-(xi) or (xiii). In effect, the Examiner is trying to use the nebulized or liquid size of Foulds in order to modify a particle size of a solid as in the claimed invention. Such "apples and oranges" combination do not make a prima facie case of obviousness for the claimed invention.

Furthermore, the Examiner only "assumes" (page 13, lines 7-10) of the preceding Office Action that 100% of Meade's particles fall between 1 and 5μm "because Meade et al are silent on the percentage of particles". If one was to use "silence" of a reference as supporting an "assumption" that the claimed invention is taught, then no invention would be patentable because documents can always be found which are found "silent" on the features of the claimed invention.

Rather, the Examiner has the initial burden of providing the factual features of the claimed invention and may not resort to speculation, unfounded assumptions or hindsight as a substitute.

Rejections based on 35 U.S.C. Section 103 must rest on a factual basis; *In re Warner* 379 F.2d 1011 (CCPA 1967). Therein, the court stated, *Warner, supra* at 1017:

"In making such rejections, the Examiner has the initial duty of supplying the requisite factual basis and may not, because of doubts that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply

deficiencies on the factual basis" (emphasis added).

Because Foulds et al does not teach that solid formulations having small particle size are necessary, since he nebulizes a liquid e.g. a solution, the particle sizes could be of any size before being dissolved into the solution and, being subsequently dissolved into the solution, particle size of the original particle has no description in Foulds et al. Thus, the liquid being nebulized in Foulds et al has no technical correspondence to the solid particles being utilized in the composition of the claimed invention. Thus, applicants respectfully submit that one of ordinary skill in the art would not have been motivated to formulate a solid composition in a finely divided particulate form as specified in the claimed invention in view of the proposed combination of Meade and Foulds et al.

Furthermore, applicants again reiterate that the previous Declaration submitted under 37 CFR 1.132 of Geena Malhotra demonstrates that triple combination appear to defy the effect of agglomeration over time over single and double comparative formulations. Of course "agglomeration" of a minutely divided liquid or nebulized dosage as in Foulds et al. is incomprehensible in Foulds as liquids do not agglomerate. As only solids can agglomerate, and there is no teaching in Meade et al. (even as modified with Foulds et al) against agglomeration applicants again reiterate that the showings in the Malhotra Declaration do provide both unobvious and unexpected properties over the cited references of the rejection. For all the foregoing reasons, withdrawal of the rejection is respectfully requested.

Reconsideration of the alternative rejection of claims 1-9, 15-22 and 24-26 under 35 U.S.C. 103 (a) as being unpatentable over Keller et al (U.S. Patent 6,645,466 B1) in view of Foulds et al is respectfully requested.

As previously noted, Keller et al is concerned with the problem of poor moisture resistance of dry powder formulations and Keller et al is not directed to any particular combination of active ingredients, but rather to the general principle of using magnesium

stearate in a dry powder inhalation (DPI) formulation. Although various active ingredients are mentioned, such is only in passing, particular actives/combination of active ingredients are irrelevant to the invention of Keller et al. Thus, a skilled person would not have looked to this document in providing formulations of the specific kind and especially the elected species as Keller simply does not relate to the field to which the present invention relates nor have any teachings which would make obvious the instantly recited claimed subject matter which are specified as particular combinations of active ingredients, in a particulate form, having a particle size ranging from about nano-size up to about 12μm formulations for species (i)-(ix) and(xiii) and for formulation (x)-(xii) (xii being the elected species) 95% of the actives have particle size less than 2.5μm, with the remainder of the particles being in the range of 2.5-5μm. Although it is alleged that Keller et al teach a formulation that can contain 2 or more pharmaceutically active compounds, such is neither a teaching nor a suggestion of the claimed subject matter. Keller et al is simply insufficient to establish as obvious the claimed invention as the time the invention was made, even in view of Foulds et al, because as noted in the discussion of Foulds above (with regard to combination of Meade et al.) Foulds is directed to nebulized (i.e. minutely divided liquid formulations) and not to solids of a claimed particle size. While applicants specify (and exemplify) various active ingredient combinations, Keller et al does not do so. This is clearly recognized by the Examiner on page 16, first full paragraph of the preceding Office Action. However, in view of this concession, (as well as the concession on the first full paragraph on page 17 of the previous Office Action) that "because Keller et al are silent on the percentage of particles that are most 5μm, it is assumed that 100% (i.e. approximately 95% would fall in the range (of particle sizes are at most 5μm, a range that overlaps applicants invention) is pure speculation on the part of the Examiner. If the Examiner wants to assume that the silence of Keller on the particularly claimed elements means the elements are present

because of the silence, why not merely assume that the claimed subject is anticipated and be done with it? As noted above, the courts have directed the Office not to rely on unfounded assumptions and speculations but rather, place the burden upon the Examiner, as a fact finder, to find the claimed elements. Silence is not the equivalent of a teaching. For all the forgoing reasons, applicants respectfully submit that Keller and Foulds, in any possible combination, cannot establish a prima facie case of obviousness for the claimed invention. Withdrawal of the rejection is therefore respectfully requested.

Reconsideration and withdrawal of the (obvious-type double patenting) of claims 1-4, 8, 15-18, 20-22 and 24-25 over claims 1-3, 5-7, 9-10 and 12-13 of copending application number 11/574,902 in view of Meade et al is respectfully requested. The Examiner concedes (last Office Action page 9, lines 6-7) that "the conflicting claims have not in fact been patented". Because of this concession, there can be no "double patenting of the obvious type" and the requirement of a terminal disclaimer is inappropriate because there is in fact no double-patenting possible at this time with no claims being patented. Withdrawal of the rejection is therefore respectfully requested

Having fully responded to the preceding Office Action, favorable reconsideration and withdrawal of all rejections and passage of the application to issue are respectfully requested.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 14-1437, under Order No. 8693.006.US0000.

Respectfully submitted,

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Attachment:

Dorland's Illustrated Medical Dictionary

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